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Total # of Pages 16 (including this page)

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United States Patent and Trademark Office Attn: Examiner Gail Gabel; Art Unit: 1641	703-305-0807	703-308-4242

<p>From : Barry S. Wilson</p> <p>Date : September 25, 2003</p> <p>Client/Matter No : 071949-2104</p> <p>User ID No : 3067</p>

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MESSAGE:

Re: US Patent Application No. 09/349,194
Our Ref.: 071949-2104

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Attached please find:

- Transmittal (1 pg.);
- Communication to the Examiner (4 pgs.);
- Exhibit A (10 pgs.).

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PATENT 071949-2104

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: BUECHLER et al.
Title: NOVEL METHODS FOR THE ASSAY OF
TROPONIN I AND T AND COMPLEXES
OF TROPONIN I AND T AND
SELECTION OF ANTIBODIES FOR USE
IN IMMUNOASSAYS
Appl. No.: 09/349,194
Filing Date: July 7, 1999
Examiner: Gail Gabel
Art Unit: 1641

<p>CERTIFICATE OF FACSIMILE TRANSMISSION I hereby certify that this paper is being facsimile transmitted to the United States Patent and Trademark Office, Alexandria, Virginia on the date below.</p> <p><u>Germaine Sarda</u> (Printed Name)</p> <p><u><i>Germaine Sarda</i></u> (Signature)</p> <p><u>September 25, 2003</u> (Date of Deposit)</p>
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Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

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Sir:

Enclosed please find:

- ☒ [X] Communication to the Examiner (4 pages);
- ☒ [X] Exhibit A (10 pages).

Respectfully submitted,

Date September 25, 2003

By *Barry Wilson*

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Customer Number: 30542

Barry S. Wilson
Attorney for Applicant
Registration No. 39,431



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PATENT TRADEMARK OFFICE

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DLMR242706.1

10/20/03
#30

PATENT
071949-2104

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: BUECHLER et al.

Title: NOVEL METHODS FOR THE
ASSAY OF TROPONIN I AND T
AND COMPLEXES OF
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Appl. No.: 09/349,194

Filing Date: July 7, 1999

Examiner: Gail Gabel

Art Unit: 1641

COMMUNICATION TO THE EXAMINER

Commissioner for Patents
Washington, D.C. 20231

Sir:

Applicants bring to the Examiner's attention recently obtained evidence which further supports Applicant's position that the claims under Appeal are in fact enabled.

To recap, the only issue on appeal is an alleged lack of enablement with regard to claims 85-96, 102-106, and 119-133. Applicants respectfully submit that the specification, which the Examiner acknowledges is enabling with regard to a pool of antibodies that specifically bind to each form of a cardiac specific troponin isoform of interest (*i.e.*, the free isoform, the isoform in binary complexes comprising another troponin component, and the isoform in ternary complexes

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comprising two additional troponin components), is also enabling with regard to a single antibody (monoclonal antibody) that binds to each of the recited troponin forms.

During prosecution of the instant claims, Applicants provided a declaration of one of skill in the art, Dr. Kenneth F. Buechler, as evidence of enablement of the claimed invention. In the declaration, Dr. Buechler provided a reasoned scientific explanation as to why the skilled artisan, using the specification as a guide and only routine methods that are well known in the art, could practice the instantly claimed invention.

After filing an Appeal Brief in the instant case, Applicants discovered a publication by Giuliani et al., "Determination of cardiac troponin I forms in the blood of patients with acute myocardial infarction and patients receiving crystalloid or cold blood cardioplegia" *Clinical Chemistry*, 45(2): 213-222 (1999), a copy of which is attached as Exhibit A. To determine the forms of cTnI circulating in the blood stream of patients with acute MI, Giuliani et al. developed three immunoenzymatic sandwich assays. See Abstract. The first assay used a combination of two monoclonal antibodies to cTnI. *Id.* This first assay, described in greater detail in the "Materials and Methods" section (p. 215, left column) of Giuliani et al., indicates the assay is for total cTnI, including free cTnI, and complexed cTnI. According to the assay, one monoclonal antibody identified as "Ab2" is the "capture" antibody and is coated on microplates and the other monoclonal antibody identified as "Ab1" is an HRP conjugate. The specificity of the total cTnI assay is described in the "Results" section on page 216 (right column), where Giuliani et al. evaluated the ability of the first assay to detect various calibrators, including free cTnI, IC binary complex and IT binary complex and TIC ternary complex. Referring to Fig. 1 (A), Giuliani concludes that the total cTnI assay detected the free, binary complexed and ternary complexed forms of cTnI ("[W]e detected all forms of cTnI: free cTnI, the IC binary complex,

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the IT binary complex, and the TIC ternary complex.").

It is respectfully submitted that Giuliani et al. demonstrates not one but two monoclonal antibodies that each bind to cTnI as free isoform, the isoform in binary complexes comprising another troponin component, and the isoform in ternary complexes comprising two additional troponin components. The capture monoclonal antibody (Ab2) in Giuliani et al.'s total cTnI assay must have been able to detect all four forms of cTnI (free, both binary forms and ternary form) as there would have been no signal with the conjugate monoclonal antibody with all four calibrators had the capture antibody not been able to bind to each of the cTnI forms. Likewise, the conjugate monoclonal antibody (Ab1) in Giuliani et al.'s total cTnI assay also must have been able to detect all four cTnI forms (free, both binary forms and ternary form) as there would have been no signal with all four calibrators if the conjugate monoclonal antibody was unable to react with each cTnI form.

Giuliani et al., therefore, proves that Applicants' method of making even a single monoclonal antibody that binds to all forms (free, binary and ternary) of cTnI is feasible without undue experimentation. In view of the above, Applicant respectfully requests that the Examiner reconsider and withdraw the enablement rejection.

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Conclusion

For the reasons discussed above, Appellants respectfully submit that all the claims are in condition for allowance, and respectfully request that the rejections be withdrawn or reversed, and that the claims be allowed to issue.

Respectfully submitted,

Date September 25, 2003

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